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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,158	01/23/2004	Sylvie Genard	LOREAL 3.0-066 (M874US)	8139

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EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

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02/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,158	GENARD, SYLVIE	
	Examiner	Art Unit	
	MAURY AUDET	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 27-46* is/are pending in the application.

4a) Of the above claim(s) *20-25 and 29-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *1-19,27,28 and 46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 March 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response and amendment are acknowledged.

Election/Restrictions

As indicated previously, Applicant's election of Group I in the reply filed on 6/26/06 (Original Restriction requirement under former Examiner Shirali) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). A second supplemental Restriction requirement was sent by this Examiner on 9/25/06, including an election of species. Thereafter, on 12/12/06, via Interview, the Examiner rejoined Group II with Group I, such that this is now the elected invention (collectively now Group I, claims 1-19, 27-28, 32-38, and 45). Additionally, a species election as to a method of making a complete identified compound species of Formula I was required, to which Applicant elected the compound shown on page 3 of the restriction response of 12/18/06. Claims 1-19 and 27-28 read on the elected species.

Claims 20-26 and 29-45 are withdrawn from consideration as being withdrawn from non-elected species (claims 32-38 and 45) or invention (claims 20-26 and 29-44). Claims 1-19 and 27-28 are examined on the merits as drawn to the elected Group I and species.

The Invention

As indicated previously, paragraph 250 of Applicant's Published Application describes the method of preparing the presently elected/claimed invention, namely: "Synthesis of the KPV Tripeptide Diacetyl Derivate under the form of Various Salts", in its diamide form.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1-19 and 27-28 and new claim 46 under 35 U.S.C. 103(a) as being unpatentable over Lipton et al. (US 5,028,592) in view of Kauvar et al. (US 5,786,336), is maintained for the reasons of record. Applicant's arguments have been considered but are not found persuasive. Applicant's primary argument is that Lipton et al. does not teach valine-amide, but rather valine-ester. However, in the context of the rejection as made, the combination of is still deemed persuasive as obvious, relying upon Lipton et al.'s extensive contemplation of minor amino acid changes or even equivalent substitutions to carry out the same effect, in the view of the secondary reference Kauver et al.'s teaching that tripeptide amides are known in to the skilled artisan in peptide chemistry. [Based on the latter, Kauver et al. is deemed analogous peptide art, merely exemplary that tripeptides are known to be modified with amide molecules]. Applicant's arguments are not persuasive. Applicant has provided no evidence that the valine-

amide does not provide some improved effect, and therefore it is deemed to provide the equivalent effect. Since one of skill in the art is well aware of how to conjugate an amide or ester onto valine, it would have been merely an equivalent routine optimization.

Specifically, Lipton et al. teach at col's 6-7:

It is believed that many changes may be made in the amino acid sequence of the peptides of the present invention and still obtain a protein which exhibits a biologically functional equivalent pharmacologic activity. For example, it has been found by Kyte et al. (1982), J. Mol. Biol., 157:105, that certain amino acids may be substitute for other amino acids having a similar hydropathic index, and still retain the biologic activity of the protein. As displayed in the table below, amino acids are assigned a hydropathic index on the basis of their hydrophobicity and charge characteristics. It is believed that the relative hydropathic character of the amino acid determines the secondary structure of the resultant protein, which in turn defines the interaction of the protein with its receptor.

In the case of the present peptides, it is believed that biological functional equivalents may be obtained by substitution of amino acids having similar hydropathic values. As used herein, a biological functional equivalent is defined as a protein that is functionally equivalent in terms of biological functional equivalent is defined as a protein that is functionally equivalent in terms of biological activity. Thus, for example, isoleucine of leucine have a hydropathic index of +4.5 and +3.8, respectively, can be substituted for valine (+4.2), and still obtain a protein having like biological activity. Alternatively, at the other end of the scale, lysine (-3.9) can be substituted with arginine (-4.5), and so on. In general, it is believed that amino acids can be successfully substituted where such amino acid has a hydropathic score of within about +/-1 hydropathic index unit of the replaced amino acid.

The following examples illustrate experiments conducted by the present inventor to illustrate the production of the preferred tripeptide, as well as various "protected" species, and use of the tripeptide in various accepted in vivo assays which demonstrate its activity. It will be appreciated that these examples are illustrative only and variations may be made in light thereof and in light of the level of skill in the art. Thus, for example, where peptides having different sequences, or longer or shorter peptidyl length, are desired, it will be apparent to those of skill in the art that the procedures generally as set forth below may be employed. Accordingly, where the sequence arg-pro-val is desired (a biologically functional equivalent of lys-pro-val), it will be apparent that dibenzyloxycarbonyl-confugated arginine ("Z-arg") should be employed in the place of "Z-arg") . Moreover, where, for example, gly-lys-pro-val is desired, it will be apparent that "Z-gly" should be employed as the starting reagent and synthetic steps employed as set forth to sequatically add the lys, pro and val residues, respectively. These and all other modifications to achieve the various peptides are well known and will be apparent to those of skill.

Applicant also argues "that [with]an appropriate selection of the protective groups, the reagents to be used and the reaction sequence makes it possible to increase the yield, in a solution synthesis, from 33% to more than 70%." *Application,* ¶¶ [0052] and [0053]". Applicant provides no indication of what "protective groups/reagents" in the presently claimed invention have been modified versus that of Lipton et al. in order to arrive at this asserted unexpected result. Until such is clear in the record, in regards to the invention as claimed, it can only be assumed that one of skill in the peptide chemistry art at the time of the present applications filing, would have known to use these newer or different reagents since the time of Lipton et al. in order to obtain a higher yield of KPV in Lipton et al. Or a question as to whether Applicant successfully ran the method steps/compounds therein of Lipton et al. Applicant may or may not have arrived at something unexpected as concerns these steps/compounds within the method, but until a specific reagent(s)/protective group(s) is identified that has caused this increase in yield, the addition of these to obtain a higher yield in standard peptide synthesis would have been deemed suggested within the general knowledge in the peptide art and motivation associated therewith.

The addition of new claim 46 to negatively claim out that no final purification step need to applied, is simply deemed a matter of routine optimization depending on the degree of purity desired. One of skill in the art would not look to Lipton et al. and believe that a final purification step must be instituted in order to arrive at the same KPV compound created in the present method.

The rejection is repeated below for continuity of record:

Lipton et al. teaches a method of making diacetyl KPV tripeptides and salts thereof (one of a number of patents Lipton et al. have since the late 80's and into the '90's on such KPV analogs and methods of making the same), for the treatment of various cellular disorders (e.g. inflammation) (see entire document, especially abstract; col. 8, line 55+). Lipton et al. was not found to expressly teach the synthesis of a KPV tripeptide "diamide" per se.

Kauvar et al. teach the synthesis of tripeptides as well (not KPV per se) and as to the diamide form of tripeptides specifically; "It has further been found that in order to exert intracellular effects, the compounds of the invention are preferably supplied as the diamides or diesters or hybrids thereof" (col. 2, lines 37-40).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to synthesize the well known KPV tripeptide in it's diamide form in the diacetyl KPV tripeptide synthesis methods of Lipton et al. because Kauvar et al. advantageously teach the in the peptide arts it was known that the diamide form of tripeptide synthesis allows for such tripeptides to optimally exert intracellular effects and one of ordinary skill in the peptide arts would have been motivated to modify the KPV tripeptide synthesis method of Lipton et al. to incorporate the diamide form, to allow greater intracellular effects by the KPV tripeptide in the methods of using the KPV tripeptide in intracellular disorders (e.g. inflammation) described by Lipton et al.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at

the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim Observations

Applicant may wish to either put all recitations of the amino acid (e.g. Proline) either in caps or lower case for consistency. In claims 16 and 19, should "OBzl benzyl" simply be "OBzl" or "Obenzyl"?

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 2/2/2008

Cecilia Tsang
Supervisory Patent Examiner
Art Unit 1654